

16, no. 10, pp. 957-961 (October 1990) ("Pollack"). The applicants respectfully traverse each of these rejections.

To anticipate a claimed invention, a reference must teach each and every element of the claimed invention. M.P.E.P. 2129. Coleman teaches a composition for treating wrinkles and scars which contains a mixture of porcine gelatin powder (collagen), sterile saline, and ϵ -amino caproic acid, which is optionally mixed with a patient's plasma prior to injection. The fluid plasma acts as a carrier for the porcine collagen injection. The Coleman composition is marketed under the name "Fibrel®". Coleman teaches that the Fibrel® composition may be administered with or without the use of the patient's plasma as a carrier and will be equally successful at treatment of wrinkles and scars in either case.

Pollack teaches use of the same Fibrel® composition for the amelioration of facial lines and wrinkles.

Contrary to the Examiner's assertion, neither Coleman nor Pollack anticipates the claimed invention, as neither teaches an injectable material for tissue augmentation comprising cross-linked, blood plasma proteins. That the plasma carrier fluid disclosed in the references may incidentally contain blood plasma proteins is irrelevant, as such proteins are not cross-linked and therefore remain soluble. In contrast, the injectable material of the present invention contains cross-linked, blood plasma proteins which are insoluble and non-biodegradable, and can therefore act as filler to augment the treated tissue. Accordingly, because Pollack and Coleman do not teach each and every element of the claimed invention, they cannot anticipate it. It is respectfully requested that the Examiner reconsider and withdraw his § 102 rejection.

Rejection Under 35 U.S.C § 103(a) Based Upon Coleman or Pollack Taken in View of Other References.

Also in Paper No. 6, the Examiner has maintained his rejection of claims 1-22 under 35 U.S.C. § 103(a), asserting that such claims are obvious over Coleman or Pollack, each taken in view of:

- (1) Grabek *et al.*, *Analytical Biochemistry*, vol. 185, pp. 13-135 (1990) ("Grabek"); or
- (2) Wong, *Chemistry of Protein Conjugation and Cross-linking*, pp. 39-40 and 195-207 (1991) ("Wong"); or

(3) Wang *et al.*, *Journal of Parenteral Drug Assoc.*, vol. 34, no. 6, pp. 452-462 (Nov.-Dec. 1980) ("Wang").

The Examiner asserts that Grabek teaches use of crosslinking agents for the purpose of crosslinking protein-protein complexes, including use of zero-length crosslinking procedures. Wong, according to the Examiner, teaches various zero-length cross-linking reagents for the purpose of creating stable bonds between two intrinsic chemical moieties of one or more polypeptide chains. Finally, the Examiner contends that Wang teaches numerous physiologically acceptable fluids as additives for parenteral formulations, including anesthetic compounds. None teaches, discusses, or suggests use of the disclosed processes or reagents to produce an injectable material for tissue augmentation comprising cross-linked blood plasma proteins. The applicants traverse this rejection for the reasons outlined below.

To establish a *prima facie* case of obviousness based upon a combination of references, the Examiner must show: (1) that the combination of references teaches or suggests all elements of the invention as claimed; (2) that there is in the art a motivation or suggestion to make such combination; and (3) that a person of ordinary skill in the art would have a reasonable expectation that such combination would be successful.

In the present case, the Examiner has failed to satisfy all of the above requirements for a *prima facie* case of obviousness. First, none of the six combinations put forth by the Examiner teaches or suggests all of the elements of the claimed invention. As discussed in the prior section of this response, neither Coleman nor Pollack, the "primary" references, teaches an injectable material comprising cross-linked blood plasma proteins. The mere addition of the zero-length crosslinking of Grabek and/or Wong does not remedy this deficiency. Similarly, the combination of the physiologically acceptable fluids taught by Wang with the teachings of Coleman and/or Pollack, as suggested by the Examiner, does not disclose an injectable material comprising cross-linked blood plasma proteins, as required by the present invention.

Additionally, even if the Examiner's suggested combinations did teach or suggest each and every element of the claimed invention, which they do not, such combinations do not render the claimed invention obvious, for there was no motivation or suggestion in the art to combine the references as suggested by the Examiner to arrive at the present invention. Both Coleman and Pollack teach the use of collagen (porcine gelatin powder), a natural structural tissue, as a filler substance for the amelioration of skin imperfections, such as scars or wrinkles. In contrast, the present invention utilizes blood plasma proteins, ordinarily soluble and

biodegradable within the body, as the filler substance. There would have been no motivation or necessity to combine the teachings of Coleman or Pollack with those of Grabek, Wong or Wang to arrive at the present invention comprising filler crosslinked blood plasma proteins, as Coleman and Pollack already teach use of a totally different filler, namely collagen.

Finally, there is no thing to suggest that a person skilled in the art would have had a reasonable expectation of success in combining these references, particularly in view of the differences between the fillers of Coleman and Pollack, one the one hand, and the various fluids taught by the secondary references.

Accordingly, for the reasons given above, it is respectfully requested that the Examiner reconsider and withdraw his § 103 rejection.

CONCLUSION

In light of the foregoing remarks, it is respectfully submitted that the claims are patentably distinguished over all art of record and known to applicants. Reconsideration and allowance of the claims are earnestly solicited.

Respectfully submitted,

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